

commercially prepared Multiple Tissue Expression array and the Multiple Tumor Expression array (Clontech), manufacturer recommended protocols were followed.

Polyclonal antibodies were produced by immunizing mice with synthetic peptides, with the standard protocol (Yokoyama, "Current Protocols in Immunology", 2.5.1-2.5.12, John Wiley & Sons, 1991). Sera of the mice were tested for recognition of PrLZ proteins by Western blotting and immunoprecipitation. Subsequently, specific antibodies were used in IHC analysis with 1:5,000 dilution. Pre-immune sera with the same dilution were used as isotypic control.

Transfection studies with of recombinant DNA: To over-express FLGA-tagged proteins, complete coding sequence for the PrLZ and PTD52 was cloned in frame to the p3xFLAG-myc-CMV-25 vector (Sigma, St. Louis, MO) and transfected to different cell lines with the GenePorter reagent (Gene Therapy Systems, San Diego, CA). After 24 hours of incubation, transfected cells were harvested for whole cell lysate preparation. The lystates were used in immunoprecipitation and Western blotting with anti-FLAG and anti-PrLZ antibodies.

To study the subcellular distribution of the proteins, complete coding sequence for the PrLZ and TPD52 was ligated in frame to the pEGFPc1 vector (Clontech). G418 (800 µg/ml) was used to select stably transfected clones, which were isolated by limited dilution. Successful GFP fusion of the proteins was confirmed by Western blotting. Subcellular localization of the fusion protein was determined by fluorescence microscopy on tissue culture dishes, and by confocal micrograph on cover slides.

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule comprising at least 25, 50, 75, or 100 contiguous nucleotides of SEQ ID NO:1.
2. The nucleic acid molecule of claim 1, wherein the contiguous nucleotides include the guanine nucleotide at position -1 of Figure 1 (SEQ ID NO:1).
3. The nucleic acid molecule of claim 1, comprising at least 500, 1,000, 1,500, 2,000, 2,500, 3,000, 3,500, 4,000, 4,500, 5,000, 5,500, 6,000, 6,500, 7,000, 7,500, 8,000, 8,500, 9,000, 9,500, 10,000, 10,500, 11,000, or 11,500 contiguous nucleotides of SEQ ID NO:1.
4. The nucleic acid molecule of claim 3, wherein the contiguous nucleotides include the guanine nucleotide at position -1 of Figure 1 (SEQ ID NO:1).
5. The nucleic acid molecule of any of claims 1-4, wherein the nucleic acid molecule, when operably linked to a sequence that encodes a polypeptide, directs expression of the polypeptide in a cell under physiological conditions.
6. The nucleic acid molecule of any of claims 1-5, wherein the nucleic acid molecule comprises a TATA box, a CCAAT box, an Sp1 site, a TRE (TPA (12-O-tetradecanoyl-phorbol-13-acetate) response element), a CRE (cyclic AMP response element), an Ets binding site, an ERE (estrogen response element), a Myc binding site or a binding motif for Myc-Max dimers, an Nf-1 binding site (a binding site for NF1-A, NF1-B, NF1-C, or NF1-X), a GATA binding site (a binding site for one of GATA-1 to GATA-6), an E2F binding site, an LSF binding site, a Mef-2 binding site, a CarG box (also known as an SRF (serum response factor) binding site), a Myf binding site (a binding site for MyoD, myogenin, myf5 or MRF4), or a TEA/ATTS domain (a Tef (transcription enhancer factor) binding site).
7. The nucleic acid molecule of any of claims 1-5, comprising the nucleic acid sequence of SEQ ID NO:1.

8. The nucleic acid molecule of any of claims 1-5, consisting of the nucleic acid sequence of SEQ ID NO:1.
9. The nucleic acid molecule of any of claims 1-7, further comprising a sequence encoding a detectable protein, wherein the nucleic acid molecule of any of claims 1-7 is operably linked to the sequence encoding the detectable protein.
10. The nucleic acid molecule of claim 9, wherein the detectable protein is not PrLZ (Prostate Leucine Zipper).
11. The nucleic acid molecule of claim 9, wherein the detectable protein comprises a fluorescent or luminescent protein.
12. The nucleic acid molecule of claim 9, wherein the detectable protein is an enzyme that catalyzes a reaction that produces a detectable reaction product.
13. The nucleic acid molecule of claim 9, wherein the detectable protein is a metal chelator.
14. The nucleic acid molecule of any of claims 1-7, further comprising a sequence encoding a protein that inhibits the proliferation of a cell in which it is expressed, wherein the nucleic acid molecule of any of claims 1-7 is operably linked to the sequence encoding the protein that inhibits the proliferation of the cell.
15. The nucleic acid molecule of claim 14, wherein the protein that inhibits the proliferation of a cell is an apoptotic protein, a tumor suppressor factor, a protein that inhibits PrLZ expression or activity, or a toxin.
16. A vector comprising the nucleic acid molecule of any of claims 1-15.

17. The vector of claim 16, wherein the vector is a plasmid, a cosmid, a bacterial artificial chromosome (BAC), a yeast artificial chromosome (YAC), an adenovirus, an adeno-associated virus, or a retrovirus.

18. A cell comprising the isolated nucleic acid of any of claims 1-15 or the vector of claim 16 or claim 17.

19. A pharmaceutically acceptable composition comprising the nucleic acid of any of claims 1-15 or the vector of claim 16 or claim 17.

20. An antibody that specifically binds PrLZ.

21. The antibody of claim 20, wherein the antibody is a monoclonal antibody or a single chain antibody.

22. The antibody of claim 20 or claim 21, wherein the antibody is humanized.

23. An antisense oligonucleotide comprising at least 15 nucleotides having a sequence that is the reverse and complement of 15 contiguous nucleotides within the coding sequence of SEQ ID NO:2.

24. A kit for detecting PrLZ expression or altering PrLZ expression or activity in a cell, the kit comprising instructions for use and a nucleic acid molecule of any of claims 1-15, the vector of claim 16 or claim 17, the antibody of claim 20 or 21, or the antisense oligonucleotide of claim 23.

25. A method for identifying a protein that inhibits the proliferation a cell, the method comprising

(a) providing a cell comprising a vector in which the sequence of SEQ ID NO:1, or an operable portion thereof, directs the expression of a test protein in the cell and

(b) assessing the rate at which the cell proliferates following expression of the test protein, wherein a decrease in the rate of proliferation indicates that the test protein is a protein that inhibits proliferation of the cell.

26. The method of claim 25, wherein the cell is an epithelial cell.

27. The method of claim 26, wherein the epithelial cell is an epithelial cell of the prostate gland.

28. The method of any of claims 25-27, wherein the cell is a cancerous cell.

29. The method of any of claims 25-28, wherein the test protein comprises an apoptotic protein, a tumor suppressor factor, a protein that inhibits the expression or activity of PrLZ, or a toxin.

30. A method of determining whether a patient has a prostatic disease or whether a patient is at risk of developing a prostatic disease, the method comprising determining whether PrLZ expression is elevated in cells of a biological sample obtained from the patient or whether cells in a biological sample obtained from the patient contain an amplified PrLZ gene.

31. The method of claim 30, wherein the biological sample comprises prostate epithelial cells.

32. The method of claim 30, wherein the biological sample comprises blood, urine, or ejaculate.

33. A method of identifying an agent that regulates the expression of the gene encoding PrLZ, the method comprising

(a) providing a cell that contains a vector comprising SEQ ID NO:1, or an operable portion thereof, and a reporter gene, wherein the cell is maintained under conditions in which the reporter gene is expressed;

(b) exposing the cell to a test agent; and

(c) determining whether the test agent alters the expression of the reporter gene, wherein an alteration in the expression of the reporter gene indicates that the test agent regulates the expression of the gene encoding PrLZ.

34. The method of claim 33, wherein the cell is a mammalian cell.

35. The method of claim 34, wherein the mammalian cell is cancerous.

36. The method of claim 35, wherein the cancerous cell is a cancerous prostate cell.

37. The method of claim 33, wherein the cell is a cell of a cell line.

38. The method of any of claims 33-37, wherein the test agent comprises a member of a library of cDNA molecules, proteins, or small molecules.

39. A method of treating a patient who has cancer or a high grade dysplasia, the method comprising administering to the patient an agent that inhibits the expression or activity of PrLZ.

40. The method of claim 39, wherein the patient has prostate cancer or a high grade dysplasia affecting prostate cells.

41. The method of claim 39, wherein the patient has a cancer or dysplasia affecting breast cells, kidney cells, cells within the gastrointestinal tract, or any other cells that express PrLZ.

42. The method of claim 39, wherein the agent that inhibits the expression or activity of PrLZ is an anti-PrLZ antibody, an oligonucleotide having a sequence that is the reverse and complement of a portion of the PrLZ gene sequence, or an agent that inhibits an androgen receptor.

43. Use of an agent that inhibits the expression or activity of PrLZ for the treatment of cancer or high grade dysplasia.

44. Use of an agent that inhibits the expression or activity of PrLZ for the preparation of a medicament for the treatment of cancer or high grade dysplasia.

45. Use of an agent as described in claim 43 or claim 44, wherein the cancer or dysplasia affects prostate tissue, breast tissue, renal tissue, tissue within the gastrointestinal tract, or any other PrLZ-positive tissue.

46. A method of treating a patient who has cancer or a high grade dysplasia affecting a PrLZ-expressing tissue, the method comprising administering to the patient a vector comprising SEQ ID NO:1, or an operable portion thereof, and a sequence that encodes a protein that inhibits the proliferation of a cancerous cell, or a cell deemed dysplastic, within the patient.

47. The method of claim 46, wherein the cancer or high grade dysplasia affects cells in the prostate, breast, renal system, or gastrointestinal tract.

48. The method of claim 46, wherein the protein that inhibits the proliferation of a cell is an apoptotic protein, a tumor suppressor factor, a protein that inhibits PrLZ expression or activity, or a toxin.

49. Use of a vector comprising SEQ ID NO:1, or an operable portion thereof, and a sequence that encodes a protein that inhibits the proliferation of a cancerous cell or a cell deemed dysplastic in a patient for the treatment of cancer or high grade dysplasia.

50. Use of a vector comprising SEQ ID NO:1, or an operable portion thereof, and a sequence that encodes a protein that inhibits the proliferation of a cancerous cell or a cell deemed dysplastic in a patient for the manufacture of a medicament for the treatment of cancer or high grade dysplasia.

51. Use of a vector as described in claim 49 or claim 50 for the treatment of cancer or dysplasia in the prostate, breast, renal system, or gastrointestinal tract.